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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/777,517	02/12/2004	Edward Roydon Jost-Price	50164/026005	6701
21559	7590	03/20/2008		
CLARK & ELBING LLP 101 FEDERAL STREET BOSTON, MA 02110			EXAMINER PACKARD, BENJAMIN J	
			ART UNIT 1612	PAPER NUMBER
			NOTIFICATION DATE 03/20/2008	DELIVERY MODE ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

patentadministrator@clarkelbing.com

Office Action Summary	Application No. 10/777,517	Applicant(s) JOST-PRICE ET AL.	
	Examiner Benjamin Packard	Art Unit 1612	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 03 December 2007.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☐ Claim(s) 1-86 is/are pending in the application.
- 4a) Of the above claim(s) 1-24, 29, 31-44, 51-54, 59, 60, 66-80 and 82--86 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 25-28, 30, 45-50, 55-58, 61-65 and 81 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____ |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date <u>13pgs (12/27/2008)</u> | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

Election/Restrictions

Applicant's election without traverse of Group II (claims 25-50, 55-59, 61-65, and 81 drawn to a method for modulating proinflammatory cytokines) and the following species: SSRI of paroxetine, corticosteroid of prednisolone, additional agent of DMARD and disorder of rheumatoid arthritis, in the reply filed on 12/03/2007 is acknowledged.

Claims 1-24, 29, 31-44, 51-54, 59-60, 66-80 and 82-86 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected inventions and species there being no allowable generic or linking claim.

Claim Rejections - 35 USC § 112

LACK OF WRITTEN DESCRIPTION UNDER 35 U.S.C. § 112, FIRST PARAGRAPH:

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 25-28, 30, 45-50, 55-58, 61-65, and 81 are rejected under 35 U.S.C. § 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

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The description requirement of the patent statute requires a description of an invention, not an indication of a result that one might achieve if one made that invention. See, e.g. In re Wilder, 22 USPQ 369, 372-3 (Fed. Cir. 1984). (Holding that a claim was not adequately described because the specification did "little more than outline goals appellants hope the claimed invention achieve and the problems the invention will hopefully ameliorate.")

Mere indistinct terms (such as "analog" (claims 25 and 81); "glucocorticoid receptor modulator" (claim 55), "small molecular immunomodulator" and "biologic" (claims 61 and 81)), however may not suffice to meet the written description requirement. This is particularly true when a compound is claimed in purely functional terms. See Univ. of Rochester v. G.D. Searle, 69 USPQ2d 1886, 1892 (CAFC 2004), stating:

The appearance of mere indistinct words in a specification or a claim, even an original claim, does not necessarily satisfy that requirement. A description of an anti-inflammatory steroid, i.e., a steroid (a generic structural term) described even in terms of its functioning of lessening inflammation of tissues fails to distinguish any steroid from others having the same activity or function. A description of what a material does, rather than of what it is, usually does not suffice.... The disclosure must allow one skilled in the art to visualize or recognize the identity of the subject matter purportedly described. (Emphasis added).

A description of a chemical genus will usually comprise a recitation of structural features common to the members of the genus, which features constitute a substantial portion of the genus. See University of California v. Eli Lilly and Co., 43 USPQ2d 1398, 1406 (Fed. Cir. 1997). This is analogous to enablement of a genus under section 112, P 1, by showing the enablement of a representative number of species within the genus.

A chemical genus can be adequately described if the disclosure presents a sufficient number of representative species that encompass the genus. If the genus has

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substantial variance, the disclosure must describe a sufficient number of species to reflect the variation within that genus. See MPEP 2163. Although the MPEP does not specifically define what constitutes a representative number of species, the courts have indicated what does not constitute the same. See, e.g., In re Gostelli, 10 USPQ2d 1614, 1618 (Fed. Cir. 1989), holding that the disclosure of two chemical compounds within a subgenus did not adequately describe such subgenus.

The MPEP lists factors that can be used to determine if sufficient evidence of possession has been furnished in the disclosure of the Application. These include the level of skill and knowledge in the art, partial structure, physical and/or chemical properties, functional characteristics alone or coupled with a known or disclosed correlation between structure and function, and the method of making the claimed invention. Disclosure of any combination of such identifying characteristics that distinguish the claimed invention from other materials and would lead one of skill in the art to the conclusion that the applicant was in possession of the claimed species is sufficient. MPEP 2163.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 25-28, 30, 45-50, 55-58, 61-65, and 81 are rejected under 35

U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Specifically,

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the term "analog" (claims 25 and 81), while having three possible examples in the instant specification (paragraph 8), does not particularly point out and distinctly claim what the class of "analog" would be.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 25-28,30,45-50,55-58,61-65 and 81 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for reduction of certain secretions in vitro, does not reasonably provide enablement for treating the broader immunoinflammatory disorders (e.g., claim 26), or decreasing cytokine secretion (e.g., claim 25) *in vitro* or *in vitro*. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to practice the invention commensurate in scope with these claims.

To be enabling, the specification of the patent must teach those skilled in the art how to make and use the full scope of the claimed invention without undue experimentation. In *re Wright*, 999 F.2d 1557, 1561 (Fed. Cir. 1993). Explaining what is meant by "undue experimentation," the Federal Circuit has stated:

The test is not merely quantitative, since a considerable amount of experimentation is permissible, if it is merely routine, or if the specification in question provides a reasonable amount of guidance with respect to the direction in which the experimentation should proceed to enable the determination of how to practice a desired embodiment of the claimed invention. *PPG v. Guardian*, 75 F.3d 1558, 1564 (Fed. Cir. 1996).

The factors that may be considered in determining whether a disclosure would require undue experimentation are set forth by *In re Wands*, 8 USPQ2d 1400 (CAFC 1988) at 1404 where the court set forth the eight factors to consider when assessing if a disclosure would have required undue experimentation. Citing *Ex parte Forman*, 230 USPQ 546 (BdApls 1986) at 547 the court recited eight factors:

- 1) the quantity of experimentation necessary,
- 2) the amount of direction or guidance provided,
- 3) the presence or absence of working examples,
- 4) the nature of the invention,
- 5) the state of the prior art,
- 6) the relative skill of those in the art,
- 7) the predictability of the art, and
- 8) the breadth of the claims.

These factors are always applied against the background understanding that scope of enablement varies inversely with the degree of unpredictability involved. In *re Fisher*, 57 CCPA 1099, 1108, 427 F.2d 833, 839, 166 USPQ 18, 24 (1970). Keeping that in mind, all *Wands* factors have been considered and the following factors that are relevant to the instant fact situation for the following reasons:

1. The nature of the invention, state and predictability of the art, and relative skill level

The invention relates to treatment of disease, particularly treating immunoinflammatory disorders (e.g., claim 26), or decreasing cytokine secretion (e.g.,

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claim 25) *in vitro* or *in vitro*. The relative skill of those in the art is high, that of an MD or PHD. That factor is outweighed, however, by the unpredictable nature of the art. As illustrative of the state of the art, the examiner cites Bymaster et al, *Europsycho pharmacology*, 2001, VOL.25,NO.6, pgs 871-880. Bymaster et al teach at page 876 the unpredictability of duloxetine compared to venlafaxine (SSRI inhibitors) during *in vitro* and *in vivo* testing, given the complex nature of immunological interactions and the vast array of molecules involved. Moreover, the class of "SSRI" compounds is huge, covering species having many divergent structures. The specification does not appear to provide an adequate correlation between structure and function, such that the invention, as least as recited in the broader claims, would not appear to be adequately enabled.

2. The breadth of the claims

The claim relates to treating immunoinflammatory disorders and decreasing cytokine secretion.

3. The amount of direction or guidance provided and the presence or absence of working examples

The specification provides no direction or guidance for treatment of the many possible cancers. No reasonably specific guidance is provided concerning useful therapeutic protocols for disorders, other than the compounds specifically tested for in

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vivo effect, such as in working example 5, fluoxetine, fluvoxamine, etc. The latter is corroborated by the working examples.

4. The quantity of experimentation necessary

Because of the known unpredictability of the art, and in the absence of experimental evidence, no one skilled in the art would accept the assertion that the instantly claimed agents could be predictably used for treatment of the many possible cancers as inferred by the claim and contemplated by the specification. Accordingly, the instant claims do not comply with the enablement requirement of §112, since to practice the invention claimed in the patent a person of ordinary skill in the art would have to engage in undue experimentation, with no assurance of success.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.

4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary.

Claims 25-28, 30, 45-50, 55-58, 61-65, and 81 are rejected under 35 U.S.C. 103(a) as being unpatentable over Siegel et al (US Patent 6,204,245, see applicants IDS dated 12/27/2007).

Siegel et al teaches a method of decreasing proinflammatory cytokine secretion or production in patents with autoimmune disease (column 5 lines 27-49) with a common mechanism of rheumatoid arthritis (column 2 lines 34-41) by use of an immunosuppressive agent, including the glucocorticoid prednisolone in combination with the selective serotonin reuptake inhibitor (SSRI) paroxetine (column 3, line 49 to column 4 line 27). The addition of methotrexate is also taught (column 7 lines 22-24).

The specific combination of features claimed is disclosed within the broad generic ranges taught by the reference but such "picking and choosing" within several variables does not necessarily give rise to anticipation. Corning Glass Works v. Sumitomo Elec., 868 F.2d 1251, 1262 (Fed. Circ. 1989). Where, as here, the reference does not provide any motivation to select this specific combination of variables, anticipation cannot be found.

That being said, however, it must be remembered that "[w]hen a patent simply arranges old elements with each performing the same function it had been known to

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perform and yields no more than one would expect from such an arrangement, the combination is obvious”. KSR v. Teleflex, 127 S.Ct. 1727, 1740 (2007)(quoting Sakraida v. A.G. Pro, 425 U.S. 273, 282 (1976). “[W]hen the question is whether a patent claiming the combination of elements of prior art is obvious”, the relevant question is “whether the improvement is more than the predictable use of prior art elements according to their established functions.” (Id.). Addressing the issue of obviousness, the Supreme Court noted that the analysis under 35 USC 103 “need not seek out precise teachings directed to the specific subject matter of the challenged claim, for a court can take account of the inferences and creative steps that a person of ordinary skill in the art would employ.” KSR v. Teleflex, 127 S.Ct. 1727, 1741 (2007). The Court emphasized that “[a] person of ordinary skill is... a person of ordinary creativity, not an automaton.” Id. at 1742.

Consistent with this reasoning, it would have obvious to have selected various combinations of various disclosed ingredients from within a prior art disclosure, to arrive compositions “yielding no more than one would expect from such an arrangement”.

Additionally, the dosage amount and sequencing would be obvious to one of ordinary skill in the art where the instantly claimed range is from “low dosage” to “high dosage”.

Claims 25-28, 30, 45-50, 55-58, 61-65, and 81 are rejected under 35 U.S.C. 103(a) as being unpatentable over Shi et al (US Pregrant Pub 2002/0012966).

Shi et al teaches the treatment of various diseases treatable by polypeptides of the application such as rheumatoid arthritis (paragraph 681), in combination with other agents, such as prednisolone, methotrexate, HYDELTRASOL.TM. (prednisolone), FOLEX.TM. (paragraph 1101) and paroxetine (paragraph 1130).

The specific combination of features claimed is disclosed within the broad generic ranges taught by the reference but such “picking and choosing” within several variables does not necessarily give rise to anticipation. Corning Glass Works v. Sumitomo Elec., 868 F.2d 1251, 1262 (Fed. Circ. 1989). Where, as here, the reference does not provide any motivation to select this specific combination of variables, anticipation cannot be found.

That being said, however, it must be remembered that “[w]hen a patent simply arranges old elements with each performing the same function it had been known to perform and yields no more than one would expect from such an arrangement, the combination is obvious”. KSR v. Teleflex, 127 S.Ct. 1727, 1740 (2007)(quoting Sakraida v. A.G. Pro, 425 U.S. 273, 282 (1976). “[W]hen the question is whether a patent claiming the combination of elements of prior art is obvious”, the relevant question is “whether the improvement is more than the predictable use of prior art elements according to their established functions.” (Id.). Addressing the issue of obviousness, the Supreme Court noted that the analysis under 35 USC 103 “need not seek out precise teachings directed to the specific subject matter of the challenged claim, for a court can take account of the inferences and creative steps that a person of ordinary skill in the art would employ.” KSR v. Teleflex, 127 S.Ct. 1727, 1741 (2007).

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Consistent with this reasoning, it would have obvious to have selected various combinations of various disclosed ingredients from within a prior art disclosure, to arrive compositions “yielding no more than one would expect from such an arrangement”.

Additionally, the dosage amount and sequencing would be obvious to one of ordinary skill in the art where the instantly claimed range is from “low dosage” to “high dosage”.

Double Patenting

Claims 25-28, 30, 45-50, 55-58, 61-65, and 81 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 22-41, 49-53, and 70 of copending Application No. 10/670,488. Although the conflicting claims are not identical, they are not patentably distinct from each other because both are directed to compositions of SSRI and corticosteroids for treatment of disorders related to proinflammatory cytokines.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Conclusion

No claims allowed.

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Any inquiry concerning this communication or earlier communications from the examiner should be directed to Benjamin Packard whose telephone number is 571-270-3440. The examiner can normally be reached on M-F 8-3:45 EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Frederick Krass can be reached on 571-272-0580. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Benjamin Packard/
Patent Examiner, Art Unit 1612

/Frederick Krass/
Supervisory Patent Examiner, Art Unit 1612